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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/691,624 | 10/24/2003 | Joachim Brendel | 02481.1687-03 | 8262 |

5487 7590 04/05/2007

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| EXAMINER | |
|---|---|
| DESAI, RITA J | |
| ART UNIT | PAPER NUMBER |
| 1625 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | NOTIFICATION DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 04/05/2007 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 04/05/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/691,624 | BRENDEL ET AL. | |
| | Examiner | Art Unit | |
| | Rita J. Desai | 1625 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *18 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-8,11-14 and 23-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-6* is/are allowed.

6)☒ Claim(s) *7,8,11-14 and 23-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1-8, 11-14, 23-26 are pending.

The rejection of the claims 1-8, 11-14 and 23-26 under 35 USC 112 first paragraph still stands.

Applicants arguments that the previous parents were allowed is not found to be convincing.

Each case is based on it own merits.

The rejection is being repeated here.

Claims 11-14 and 26 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for some IC50 values using a Kv1.5 channel of zenopus oocytes, does not reasonably provide enablement for treating, termination or preventing of atrial fibrillation or flutter. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many compounds from an aromatic carbocyclic moiety to an aromatic carbocyclic moiety having many large electron withdrawing and bulky groups substituted on it to a moiety having many heterocyclic rings. These compounds cover a very wide range of compounds.

2) The nature of the invention: The invention is a (highly) substituted biphenyl compound that is useful in pharmaceuticals.

3) The state of the prior art: The state of the prior art is that it involves screening in vitro and invivo to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability and no established correlation between in vitro activity and the

treatment or prevention of atrial fibrillation and in vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art. There is also not relationship The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The level of unpredictability is in the art is very high. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group.

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. There are no examples providing data to show that these compounds do indeed treat treat atrial fibrillation or even prevent the re occurrence of it. The only data provided is the IC50 values for using a Kv1.5 channel of zenopus oocytes,

7) The lack of existence of working examples: The instant specification does not have any working examples. There is no in vivo data , nor any population data that it does in fact treat arrythymia.

8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are no working examples, the amount of experimentation is very high and burdensome.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention for the treatment or even for the prevention of atrial fibrillation.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

"A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable."

Compounds according to the invention have been made. The assay test is noted. While screening test in an enzyme assay provides data in picking and choosing lead compounds for further testing, screening test per se does not provide sufficient operational guidance in an "individual" in patho-physiological environment.

Applicants arguments :-

The specifications on page 2 lines 16-19 states that the claimed compounds act on Kv1.5 potassium channel and inhibit potassium current described as "ultra rapidly activating delayed rectifier" in human atrium.

This may be so however there is no data in the specification that the compounds invivo do treat arrythymia.

Abstract , Thorac Cardiovasc Surg 2002, Feb. 19 2002 Knobloch et al clearly indicates that further clinical studies need to be done. Thus at the time the invention was filed it was not art accepted that Kv1.5 had any effect on arrhythmia and hence when the predictability in the art is low , one should provide more guidance regarding the activity and treatment or prevention of arrhythmia or atrial fibrillation.

The compounds of claims 7 and 8 are "pharmaceutical" compositions and as such treat an disorder which is not enabled in the specifications and hence are rejected.

Thus the rejection still stands.

The objection to the claims 1-5 has been withdrawn as applicants have clearly indicated the difference between them.

***Conclusion***

Claims 7,8 11-14 and 23-26 are rejected.

Claims 1-6 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rita J. Desai
Primary Examiner
Art Unit 1625

R.D.
March 29, 2007

RDesai 3/29/07